Title: **Study of pharmacology and function of binding sites of nicotinic acetylcholine receptors**

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Abstract:

Nicotinic acetylcholine receptors (nAChRs) are ligand-gated ion channels. We use the whole-cell patch-clamp technique to study functional and pharmacological properties of muscle and neuronal nicotinic receptors. Rat neuronal receptors were heterologously expressed in COS cells and human embryonic muscle receptors were studied in TE671 cells.

Lobeline, a plant alkaloid with a long history of therapeutic use, interacts with the classical agonist-binding site of nAChRs. The final result of this interaction depends on the receptor subtype, lobeline and other agonists concentrations and the time schedule of application. Generally, lobeline is a very weak partial agonist eliciting deep desensitization at several subtypes of nAChRs. In combination with other agonists, lobeline acts as a competitive antagonist or coagonist.

Using point mutation procedure we studied the functional role of negatively charged amino acids in the F-loop of β2 and β4 subunits of neuronal receptors. Neutralising mutations in β4 subunit led to up to eighteen-fold increase in the EC_{50} value, slowed down the receptors desensitization and accelerated resensitization. In contrast to this, homologous mutations in β2 subunit influenced the receptor activation to a lesser extent, suggesting of a different role of the F-loop in the activation of receptors containing β2 and β4 subunits, respectively.

Keywords: nicotinic acetylcholine receptor, lobeline, F-loop